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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Application of:	Flechtner et al.	Confirmation No.:	4151
Serial No.:	10/776,521	Art Unit:	1648
Filed:	February 12, 2004	Examiner:	Blumel, Benjamin P.
For:	HEAT SHOCK PROTEIN-BASED VACCINES AND IMMUNOTHERAPIES	Attorney Docket No:	8449-405-999

DECLARATION OF MICHAEL A. YAMIN, PH.D. UNDER 37 C.F.R. § 1.132

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

I, Michael A. Yamin, do declare that:

1. I am a citizen of the United States of America residing at 31 Heyhoe Woods Road, Palisades, New York.

2. I currently hold the position of Director of Technology Development at Warren Pharmaceuticals, Inc. having a place of business in Yorktown Heights, New York.

3. I received a Ph.D. degree in Microbiology from Rockefeller University and a B.S. degree in Bacteriology from the University of California – Davis.

4. I am a Registered Patent Agent (Reg. No. 44,414).

5. I held the position of Director of Intellectual Property and Licensing from 2001 to 2003, and the position of Consultant from 2003 to 2004, at Mojave Therapeutics, Inc. ("Mojave"). As Director of Intellectual Property and Licensing, I managed all of Mojave's intellectual property matters, including the preparation of new patent applications,

and licensing efforts. As Consultant, I managed the intellectual property portfolio. My experience and honors are set forth in my *resume*, attached hereto as Exhibit 1.

6. In July of 2004, the intellectual property assets of Mojave, the original Assignee of the above-identified patent application, were acquired by Antigenics, Inc. ("Antigenics"), which has a place of business in Lexington, Massachusetts. I understand that Antigenics is the present owner of the entire right, title and interest in, to and under the invention described and claimed in the above-identified patent application.

7. I was involved in preparing the above-identified application, United States ("U.S.") Patent Application No. 10/776,521 ("the '521 application") entitled "Heat Shock Protein-Based Vaccines and Immunotherapies" filed on February 14, 2004. I also was involved in preparing the provisional applications to which the '521 application claims priority.

8. The claims of the '521 application are directed to a hybrid antigen comprising at least one antigenic domain of an infectious agent or tumor antigen and a binding domain that non-covalently binds to a heat shock protein, optionally with a peptide linker separating the antigenic domain and binding domain, wherein the binding domain comprises the amino acid sequence Asn Leu Leu Arg Leu Thr Gly Trp ("NLLRLTGW"), Phe Tyr Gln Leu Ala Leu Thr Trp ("FYQLALTW"), or Arg Lys Leu Phe Phe Asn Leu Arg Trp ("RKLFFNLRW"); compositions comprising at least one such hybrid antigen and a pharmaceutically acceptable carrier; compositions comprising a non-covalent complex of at least one such hybrid antigen and at least one heat shock protein; and methods of inducing an immune response to a tumor antigen or an infectious agent or methods of treating an infectious disease or cancer comprising administering at least one such hybrid antigen, optionally bound non-covalently to at least one heat shock protein.

9. I have reviewed and understand the '521 application and the reference Wieland et al., U.S. Application Publication No. US 2004/0071656 A1 ("Wieland et al."), which is the publication of U.S. Application No. 10/328,953 ("the Wieland application") filed on December 23, 2002. I understand that in an Office Action dated September 21, 2006, the Examiner has rejected the claims under consideration as lacking novelty in view of Wieland et al. The Wieland application claims benefit of provisional applications filed on December 26, 2001, December 27, 2001, April 12, 2002, July 29, 2002, and September 28, 2002, respectively.

10. I also was involved in preparing the Wieland application, which was originally assigned to Mojave. I also was involved in preparing the provisional applications to which the Wieland application claims priority.

11. Wieland et al. discloses a complex of a heat shock protein and a hybrid antigen, the hybrid antigen comprising an antigenic domain, a heat shock protein binding domain, and optionally a short peptide linker interposed therebetween (*see* Wieland et al. at ¶20). In particular, the heat shock protein binding domain can comprise the amino acid sequence NLLRLTGW, FYQLALTW, or RKLFFNLRW (*see* Wieland et al. at ¶¶129-130).

12. The amino acid sequences NLLRLTGW, FYQLALTW, and RKLFFNLRW as heat shock protein binding peptides for use in covalent conjugation, optionally via a peptide linker, to an antigen to generate a hybrid antigen, optionally complexed non-covalently to heat shock protein, as well as the uses of such hybrid antigens and complexes in methods of inducing an immune response to a tumor antigen or an infectious agent or methods of treating an infectious disease or cancer were disclosed to me by Dr. Sunil Mehta prior to December 26, 2001, for purposes of preparing U.S. Provisional Application No. 60/447,142 filed on February 13, 2003, and subsequently the '521 application and its other priority applications. As evidence of this disclosure, attached hereto as Exhibit 2 is a copy

of an e-mail from Dr. Sunil Mehta to me disclosing the amino acid sequences, dissociation constants ("Kds") for binding to Hsp70, heat shock proteins the peptides are disclosed to bind to (in the respective listed publications), and other related information for the peptides S-Jav1 (NLLRLTGW), S-Jav2 (FYQLALTW), and S-Jav3 (RKLFFNLRW), which were for use in generating hybrid antigens. Although the date of the e-mail has been blanked-out, such date is prior to December 26, 2001.

13. I used the information in Exhibit 2 along with other disclosures provided by Dr. Paul Slusarewicz and other members of Dr. Slusarewicz's research group to prepare provisional applications to which the '521 application claims priority, and subsequently the '521 application, with the assistance of outside patent counsel.

14. Since I also was involved in preparing the Wieland application and the provisional applications to which the Wieland application claims priority, I incorporated the idea of using peptides having the amino acid sequence NLLRLTGW, FYQLALTW, or RKLFFNLRW as a heat shock protein binding domain to generate hybrid antigens non-covalently complexed to heat shock proteins into the specification of U.S. Provisional Application No. 60/414,834 filed on September 28, 2002 and subsequently into the specification of the Wieland application.

15. I also was involved in establishing a plan for a research collaboration ("the Collaboration") in 2002 between (a) Mojave, and (b) Drs. Felix Wieland and Franz-Ulrich Hartl (the inventors of the Wieland application) and members of their research groups. In furtherance of the Collaboration, it was intended that Mojave supply its collaborators with peptides with high affinity binding to Hsp70.

16. Attached hereto as Exhibit 3, is a copy of my handwritten note which evidenced that I disclosed the NLLRLTGW amino acid sequence of the S-Jav1 peptide to Thalia Becker, a Ph.D. student of Dr. Felix Wieland at the time and one of the Mojave

collaborators of the Collaboration. This disclosure was pursuant to a confidentiality agreement. Although the date on the handwritten note has been blanked out, such date is prior to September 28, 2002. Exhibit 3 serves as evidence of an occasion prior to September 28, 2002 when I communicated the idea of using peptides having the amino acid sequence NLLRLTGW as a heat shock protein binding domain to generate hybrid antigens non-covalently complexed to heat shock proteins as described and claimed in the '521 application to a member of Dr. Wieland's research team.

17. Thus, I (i) disclosed the idea of using peptides having the amino acid sequence NLLRLTGW as a heat shock protein binding domain to generate hybrid antigens non-covalently complexed to heat shock proteins as described and claimed in the '521 application to Thalia Becker, a Ph.D. student of Dr. Wieland; and (ii) incorporated into the specification of U.S. Provisional Application No. 60/414,834 filed on September 28, 2002 and subsequently into the specification of the Wieland application the disclosure of using peptides having the amino acid sequence NLLRLTGW, FYQLALTW, or RKLFFNLRW as a heat shock protein binding domain to generate hybrid antigens non-covalently complexed to heat shock proteins, as described and claimed in the '521 application.

18. Insofar as the invention of the pending '521 application is suggested or disclosed by anything contained in Wieland et al., such invention was (i) described to me by Dr. Sunil Metha prior to December 26, 2001; (ii) disclosed to the inventors of the Wieland application, Drs. Felix Wieland and Franz-Ulrich Hartl, or a member of their research teams prior to September 28, 2002 by me; and (iii) incorporated by me into the specification of U.S. Provisional Application No. 60/414,834 filed on September 28, 2002 and subsequently into the specification of the Wieland application.

19. I declare further that all statements made in this Declaration of my knowledge are true and that all statements made on information and belief are believed to

be true and further that these statements are made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

Date: 9/14/07

Michael A. Yamin, Ph.D.

Attachments:

Exhibit 1: *Resume* of Michael A. Yamin, Ph.D.
Exhibit 2: E-mail from Sunil Mehta to Michael A. Yamin
Exhibit 3: Handwritten Note of Michael A. Yamin

MICHAEL A. YAMIN, PH.D.

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Versatile biotech/pharma professional focused on the interface between discovery, development and financing

POSITIONS HELD

WARREN PHARMACEUTICALS, INC., Yorktown Heights, New York **2003-present**

Privately-held biotechnology company discovering and developing tissue protective compounds to treat devastating illness and injury, including stroke, spinal cord injury, heart attack, and retinopathy

Director, Technology Development

- Responsible for the company's manufacturing, preclinical and clinical development programs
- Participate in licensing, strategic partnering and fund-raising activities
- Created private placement memorandum
- Manage external research collaborations through research contracts and MTAs
- Assist in patent prosecution *(wrote all of company's initial patent applications)*

ANGION BIOMEDICA CORP., Manhasset, New York **2001-present**

Privately-held biotechnology company pursuing small molecule anti-apoptotic compounds and anti-cancer compounds targeting the hepatocyte growth factor receptor, c-met

Research Associate, 2005-present

- Direct ongoing patent strategy; oversee prosecution; prepare new patent applications
- Participate in due diligence sessions supporting IP estate
- Work with outside patent counsel on US and foreign prosecution
- Conduct competitive intelligence and asset valuations
- Write SBIR grant applications

Consultant, 2001-2005

- Wrote all of company's initial small molecule patent applications
- Directed all aspects of IP strategy

MOJAVE THERAPEUTICS, INC., Hawthorne, New York **2001-2004**

A development-stage immunotherapeutics company spun out of Memorial Sloan-Kettering Cancer Center; sold to Antigenics, Inc. in 2004.

Consultant, 2003-2004

- Managed IP portfolio during transition and intellectual assets sale

Director of Intellectual Property and Licensing, 2001-2003

- Led all matters relating to IP, including strategy, portfolio management; prepared new patent applications
- Worked in cross-functional teams with finance, regulatory and business development to solve issues related to licensing and clinical trials strategy
- Oversaw in-licensing efforts for product components
- Participated in presentations to investors and support IP due diligence

KLAUBER & JACKSON, Hackensack, New Jersey **1997-2001**

Intellectual property law firm specializing in life sciences

Patent Agent, 1999-2001

Technical Advisor, 1997-1998

- Prepared and prosecuted patent applications for biotech, pharma and academic clients

POSITIONS HELD (CONTINUED)

THE PICOWER INSTITUTE FOR MEDICAL RESEARCH, Manhasset, New York **1995-1997**
Not-for-profit biomedical research institution focused on translational biomedical research
Associate Professor; Director of Grants Administration
- Managed institutional grant process; wrote NIH and foundation applications

INNAPHARMA, INC., Suffern, New York **1994-1995**
A pharmaceutical research and development company and CRO.
Director, Licensing and Acquisition
- Evaluated technologies for potential in-licensing

ALTEON INC., Northvale, New Jersey **1987-1994**
A development-stage pharmaceutical company that discovers, develops, and commercializes therapeutic and diagnostic products for diabetes and aging. Spun out from Rockefeller University.
Vice President, Science and Technology, 1993-1994
Vice President and Scientific Director, 1987-1993
Co-Founder, 1986
- Hired administrative and research staff; oversaw new construction of lab, office and animal facility
- Directed chemistry, biochemistry, immunology, and preclinical development
- Participated in strategic partnering, public offering, and investor presentations
- Managed IP estate

THE ROCKEFELLER UNIVERSITY, New York, New York **1985-1987**
Laboratory of Medical Biochemistry, studying diabetic complications and septic shock
Research Associate
- Developed ELISA to measure TNF in human tissues and bodily fluids
- Pursued new treatment for diabetic complications and assays for nonenzymatic glycosylation products

EVREKA INC., Bergenfield, New Jersey **1982-1985**
A biomedical research and development consulting firm.
Vice President and Director of Research
- Developed prototypes of novel diagnostic devices

BOSTON UNIVERSITY, Marine Program, Woods Hole, Massachusetts **1980-1981**
Cell biology laboratory of Sidney Tamm,
Research Associate, Department of Biological Sciences
- Conducted research in cell motility

EDUCATION

Patent Agent U.S. Patent and Trademark Office. Reg. No. 44,414.

Ph.D. The Rockefeller University, New York, New York. Microbiology.

B.S. University of California, Davis, California. Bacteriology.

PROFESSIONAL MEMBERSHIPS

American Society for Biochemistry and Molecular Biology
Association of University Technology Managers
Licensing Executives Society

Michael Yamin

[redacted]

From: Sunil Metha

Sent:

To: Michael Yamin; Mee Hoe

Subject: S-Javs

Dear Michael and Mee: Here is the information about the S-Javs. If you have any questions, please let me know.

Thanks

Name	Sequence	Kd (μM) for KHSP70	Originally Checked for	Reference
S-Jav1	NLLRLTGW*	1.8	DnaK/Hsc70	J. Mol. Biol. (1994) **241**, 133-135; J. Mol. Biol. (1994) **235**, 848-854
S-Jav2	FYQLALTW*	6.0	DnaK/Hsc70	J. Biol. Chem. (1994) **269**, 30470-30478
S-Jav3	RKLFFNLRW*	23.0	DnaK	J. Mol. Biol. (1996) **256**, 829-837
S-Jav4	KLLLLLLW*	Solublization problems	Designed	Based on the predicted consensus sequence.
GSG-Jav	GSGHWDFAWPW	120	Bip	Mojave Therapeutics; Cell (1993) **75**, 717-728

tryptophan was added at the C-terminus to facilitate the quantitation of these peptides.

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Word -
password is
elephant

Thalia

Told her sequence

J1 → NLLRLTGW

GSG ASN Leu Leu ARG Leu Thr Gly Trp

[redacted] [redacted] ? [redacted]

German

Spare some J1 ??